REMARKS

Claims 1-9 remain pending. Claims 10-31 have been canceled. Claims 32-47 have been added.

Claims 32-36 finds support in the specification at page 2 lines 3, 12, and 33; page 3 line 5; and page 20 line 13. Claims 37-40 find support in the specification at page 13 lines 22-26 and page 1 lines 26-28. Claims 41-44 find support in the specification at page 11 lines 13, 15, and 28. Claims 45-46 find support in the specification at page 12 lines 34-35. Claim 47 finds support in the specification at page 13 line 2.

REJECTION OF CLAIMS 1-9 UNDER 35 U.S.C. §103(A)

Reconsideration is requested of the rejection of claims 1-9 under 35 U.S.C. § 103(a) over Massey et al.

The burden of establishing a prima facie case of unpatentability lies with the Patent and Trademark Office.[1] A prima facie case of nonobviousness is only established when the Office provides (i) one or more references (ii) available to the inventor (iii) that teach (iv) a suggestion to combine or modify the references, (v) the combination or modification of which would appear to be sufficient to have made the claimed invention obvious to one of ordinary skill in the art.[2] Thus, the Office must explain why the prior art would "appear to show the *claimed subject matter*," and not simply the general aspects of the invention.[3] If the examination at the initial stage does not produce a prima facie case of unpatentability, then without more the applicant is entitled a grant of the patent.[4]

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[1] *In re King*, 801 F.2d 1324, 1327, 231 USPQ 136, 138-39 (Fed. Cir. 1986).
[2] *See In re Lintner*, 458 F.2d 1013, 173 USPQ 560, 562 (C.C.P.A. 1972); *In re Fielder*, 471 F.2d 640, 176 USPQ 300, 302 (C.C.P.A. 1973).
[3] *In re Rhinehart*, 531 F.2d 1048, 189 USPQ 143, 147 (C.C.P.A. 1976).
[4] *In re Oetiker*, 977 F.2d 1443, 24 USPQ 2d 1443 (Fed. Cir. 1992).

A. Massey et al. neither teach or suggest a fungus cell as a target cell

Applicant's claim 1 requires, *inter alia*, selecting the non-immunoglobulin peptides from those polypeptides that specifically bind to a **target fungus**. As such, it is clear that the target cells of claim 1 are limited to fungal cells.

1. Massey et al. do not teach a fungus as a target cell

Target cells of Massey et al. are limited to cells infected with a pathogen and not the pathogen itself. Massey et al. disclose a method of identifying a peptide from a peptide library transfected into a vector and introduced into a host, then reacting the displayed peptide with a *target cell*. Massey et al. summarize their invention as follows: "The present invention provides a method for mediating killing, inhibition and/or removal of a target cell, for example, ... a pathogen-infected cell ... from the body of a patient or animal."[5] Massey et al. further provide that a "target cell can be ... a **pathogen-infected cell** .... The pathogen or parasite can be viral, bacterial, fungal, or protozoan."[6] These passages demonstrate that the target cells of Massey et al. are always those native in the body of a patient that may be infected with a pathogen. Thus, the target cell of Massey et al. is <u>not</u> the pathogen itself.

That Massey et al. do not teach a fungal target cell is supported by claim 4 of Massey et al. In claim 4, Massey recites that "the target cell is a cell infected with a virus, a bacterium, a fungus or a protozoan." In other words, the target cell is a cell infected with a virus, a cell infected with a bacterium, a cell infected with a fungus, or a cell infected with a protozoan. This interpretation is the only reasonable interpretation given that the specification of Massey et al. never discusses directly targeting fungal cells, yet repeatedly discusses targeting cells infected with a pathogen/fungus.[7]

Furthermore, Massey et al. teach away from targeting other than a pathogen infected cell. A reference teaches away when it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought

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[5] Massey et al., WO 99/51780, p. 3 ln. 28-31.
[6] *Id.* at p. 8 ln. 11-13.

by the applicant.[8] The line of development flowing from Massey et al.'s disclosure is "decorating" the native, infected target cell of a patient so that the patient's immune system will recognize it as foreign and destroy it. This line of development is unlikely to be productive in the applicant's efforts to directly target fungal pathogens of plants, a system that is devoid of any immunological response akin to that of a human.

Thus, the Office has not established a prima facie case of obviousness because Massey et al. do not teach fungal cells as target cells. This argument applies equally to claim 1 and all those claims dependent upon claim 1.

2. Massey et al. do not suggest a fungus as a target cell

Massey et al. fail to suggest modifying the disclosed methodology so as to target fungal cells directly. A prima facie case of obviousness requires some reason, suggestion, or motivation from the prior art for the person of ordinary skill to have modified the references. Targeting cells is merely a general aspect of both the Massey invention and applicant's claim 1. But Massey et al. do not "appear to show the claimed subject matter"[9] of applicant's claim 1, *i.e.*, targeting fungal cells themselves, rather than the cells which the fungus might infect. Neither is there a hint of suggestion in Massey et al. that a fungus as a target cell would be productive. Throughout Massey et al., target cells are always limited to native cells in the body of a patient that may be infected with a pathogen.

Furthermore, there is no evidence presented in Massey et al. that host cell death induced by immunological processes would lead to the death of a fungal organism contained within, or adjacent to, the cell. This is especially true for an organism that is a non-obligate parasite which can utilize dead host cell contents for growth, or for an

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[7] *See supra* nn. 4-5 and accompanying text (Massey et al. provides that a "target cell can be a tumor cell or other neoplastic cell, a parasite-infected cell or a pathogen-infected cell or a newly fertilized egg. The pathogen or parasite can be viral, bacterial, fungal, or protozoan.").

[8] *See U.S. v. Adams*, 383 U.S. 39, 52, 148 USPQ 479, 484 (1966); *W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1550-51, 220 USPQ 303, 311 (Fed. Cir. 1983), *cert. denied* 469 U.S. 851 (1984); *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 243, 245 (C.C.P.A. 1963) (reference teaches away if it leaves the impression that the product would not have the property sought by the applicant).

[9] *In re Rhinehart*, 189 USPQ at 147.

organism that produces a long-term survival structure (e.g. spore) that is not attacked by the host cell-directed antibody.

And so, the Office has not established a prima facie case of obviousness because Massey et al. provide no suggestion to target a fungal cell. This argument applies equally to claim 1 and all those claims dependent upon claim 1.

B. Massey et al. neither teach or suggest selecting non-immunoglobulin polypeptides

Applicant's claim 1 has a selection requirement that is not reflected in Massey et al. Claim 1 requires, *inter alia*, two discrete selection steps: first, isolating and sequencing those peptides (immunoglobulin or non-immunoglobulin) that bind the fungal target; and second, **"selecting the non-immunoglobulin peptides"** as a subset of the larger population of peptides that specifically bind the fungal target cell. This further selection step is not taught explicitly by Massey et al. Nor does Massey et al. suggest modifying the disclosed methodology to include the further selection step.

According to the applicant's specification, a "non-immunoglobulin peptide" is a "peptide that is not an immunoglobulin, a recognized region of an immunoglobulin, or contains a region of an immunoglobulin."[10] The common meaning of immunoglobulin includes an antibody, or a protein produced after stimulation by an antigen and acting specifically against the antigen in an immune response.[11] The Office asserts that the claims, which read on non-immunoglobulin peptides, would read on antibodies. But according to the definition provided in the specification and the common understanding of the term, "non-immunoglobulin peptides" would not read on antibodies.

1. Massey et al. do not teach selection of non-immunoglobulin peptides

In contrast to applicant's claim 1, the claims of Massey et al. teach selection of all polypeptides that bind a target cell.[12] This is further supported by Massey et al.'s

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[10] Application, p. 9 ln. 16-19.
[11] *See e.g.*, Merriam Webster Online Dictionary, 2004 <http://www.m-w.com>.
[12] Massey et al. at claim 1(b); p. 24, ln. 11-12.

definition of selected members of the polypeptide library as "those which specifically bind with some affinity or avidity to the target cell."[13]

There are at least two reasons why the class of polypeptides in Massey et al. are not the class of polypeptides in applicant's claim 1. First, because Massey et al.'s target cell is not a fungus, the polypeptides that specifically bind will be a different population of polypeptides as compared to those in applicant's claim 1. Second, even if the population of polypeptides were similar, Massey et al. fail to teach any *further selection* of a subset of all specifically binding polypeptides (*i.e.*, those non-immunoglobulin polypeptides). This further selection step is explicitly required in applicant's claim 1.

While Massey et al. disclose selection of immunogenic carriers,[14] this is a property of the carrier itself and irrelevant to the character of the isolated polypeptides.

Thus, the Office has not established a prima facie case of obviousness because Massey et al. do not teach the needed subject matter supporting the obviousness rejection, *i.e.*, selection of non-immunoglobulin peptides that bind to fungal target cells. This argument applies equally to claim 1 and all those claims dependent upon claim 1.

2. Massey et al. do not suggest selecting non-immunoglobulin peptides

A prima facie case of obviousness requires some reason, suggestion, or motivation from the prior art for the person of ordinary skill to have modified the references. The Massey et al. reference is entirely directed to selection of an immunogenic carrier with no regard to the characteristics of the polypeptides that specifically bind native, infected target cells (other than, of course, binding affinity). The binding polypeptides of Massey et al. are used merely as a tether to connect the native, infected target cell to the immunogenic carrier. The only requirement of Massey et al. in regards to the polypeptides is that they specifically bind to target cells. Massey et al. never suggest that it may be useful to select only non-immunoglobulin polypeptides—why would they when it would have no utility to their invention?

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[13] *Id.* at p. 5 ln. 25-26.
[14] *Id.* at claim 1, p. 24 ln. 22-23;

Therefore, the Office has not established a prima facie case of obviousness because Massey et al. provide no suggestion to select non-immunoglobulin peptides from the larger class of peptides that specifically bind to fungal target cells. This argument applies equally to claim 1 and all those claims dependent upon claim 1.

REJECTION OF CLAIMS 1-9 UNDER 35 U.S.C. §102(b)

Reconsideration is requested of the rejection of claims 1-4 and 6-9 under 35 U.S.C. §102(b) as being anticipated by Gough et al.[15] To satisfy prima facie anticipation, a reference must teach, expressly or inherently, each and every element required by claim 1.[16]

Claim 1 requires, *inter alia*, two discrete selection steps: first, those peptides (immunoglobulin or non-immunoglobulin) that bind the fungal target cell are isolated and sequenced; and second, **non-immunoglobulin binding peptides are selected** as a subset of the larger population of peptides that specifically bind the fungal target cell. A non-immunoglobulin peptide is:

> A peptide which is not an immunoglobulin, a recognized region of an immunoglobulin, or contains a region of an immunoglobulin. For example, **a single chain variable region of an immunoglobulin would be excluded from this definition**.[17]

Gough et al. employ a phage-displayed single-chain variable fragment (scFv) library to select antibodies specific for native external isotopes of *Phytopthora*. This scFv library is formed from human immunoglobulin V-gene domain segments.[18] So, all polypeptides in Gough et al., selected or not, are immunoglobulin polypeptide segments. Further, Gough et al. only disclose selection of immunoglobulin-fragment polypeptides that bind to *Phytopthora*.[19]

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[15] Gough et al., 1999, J. Immuno. Methods 228, 97-108.
[16] *In re Zenith*, 333 F.2d 924, 142 USPQ 158, 160 (C.C.P.A. 1964); *Celeritas Tech. v. Rockwell Intern. Corp.*, 150 F.3d 1354, 1361 (Fed. Cir., 1998).
[17] Application, p. 9 ln. 16-19.
[18] Gough et al. at 98 (referencing Vaughan et al., 1996, Nat Biotechnol. 14, 309-14).
[19] *See e.g.* Gough et al. at 98, 99.

Thus, the applicant's recited element of selecting the non-immunoglobulin peptides from those peptides binding to the fungal target is a limitation that is not found expressly in Gough et al. Neither can this step be inherent in Gough et al., for every polypeptide in the library of Gough et al. is a single chain variable region of an immunoglobulin, each of which are excluded by the limitations of applicant's claim 1.

Furthermore, Gough et al. do not recite required features of other dependent claims. For example, claims 5, 9, and 41-44 recite specific requirements of the peptides employed by various embodiments of the invention. Gough et al. disclose only single chain variable fragment (scFv) immunoglobulin peptide libraries consisting of three independent variable regions of amino acids that are constrained by the remaining scFv scaffold, where these molecules may further oligomerize.[20] Thus, Gough et al. do not disclose the required sequences of claim 5. Similarly, Gough et al. do not disclose the peptides of length 6 to 15 amino acids as required by claim 9. Also, Gough et al. do not disclose: the 8mer peptides required by claim 41; the f8-1 peptide library required by claim 42; the 15mer peptides required by claim 43; or the f88-4 peptide library required by claim 44. As another example, Gough et al. do not disclose targeting *Phytophthora sojae*, *Phytophthora capsici*, *Phytophthora palmivora*, *Phytophthora cinnamomi*, and *Phytophthora parasitica*, as required by claim 35. Similarly, Gough et al. do not disclose targeting *Phytophthora sojae* or *Phytophthora capsici*, as required by claim 36.

In summary, the Office has not established a prima facie case of anticipation by Gough et al. as against claim 1 or all such claims dependent upon claim 1, and additionally, as against claims 5, 9, 35-36, and 41-44.

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[20] Gough et al. at 98 (referencing Vaughan et al., 1996, Nat Biotechnol. 14, 309-14); *see generally* Barbas et al., 2001, Phage Display. A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY.

CONCLUSION

In light of the foregoing, applicants request: an entry of the claim amendments; request a withdrawal of claim rejections; and solicit allowance of the claims. The Office is invited to contact the undersigned attorney should any issue remain unsolved.

A check in the amount of $55.00 is enclosed for a one month extension of time. The Commissioner is hereby authorized to charge any fees which may be required for this response to Deposit Account No. 19-1345.

Respectfully submitted,

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